REMARKS

Claims 7, 9, 18 and 32-34 were pending in the application, and stand rejected.

Claims 7 and 32 are amended to recite a purified antibody or fragment thereof, which finds support, *e.g.*, at p.19, ll.11-17; p.20, ll.21-23; p.23, ll.14-15 and original Claim 15, as discussed further below.

No new matter is added by way of amendment.

I. Rejection under 35 U.S.C. §112, first paragraph

Claims 32 – 34 were rejected under 35 U.S.C. §112, first paragraph, as allegedly incorporating new matter, specifically with regard to the recitation of "residues 1-210 of SEQ ID NO: 6." It is alleged that the specification does not provide support for this limitation. However, as indicated when these claims were introduced, they find support at page 7, original Claim 2 and SEQ ID NOs: 5 and 6.[1]

The Examiner concedes that original Claim 2 encompasses the *mature* sequence of SEQ ID NO: 6 (Office Action at p.3), as currently claimed. However, there is no discussion of the disclosures at page 7 and in the sequence listing, both of which unambiguously define the amino acid residues that comprise the mature sequence of SEQ ID NO: 6. At page 7, the specification provides the amino acid sequence of FDF03-S1 "wherein the signal peptide and transmembrane domain are underlined." Specification at p.7, ll. 12-13. One of skill in the art would recognize that the signal peptide would begin at the amino terminus, with methionine (M), and thus recognize that the underlined 17 amino acids (MGRPLLLPLLLLLQPPA) was the signal peptide. He or she would also realize that this signal sequence would be cleaved during secretion to leave the remainder of the polypeptide (which correspond to residues 1 – 210 of SEQ ID NO: 6) as the mature form. The sequence listing confirms that residues 1-210 comprise the mature form of FDF03-S1. SEQ ID NO: 5 includes in its header in the field <221> the designations "sig_peptide" (386-436) and "mat_peptide" (437-1066), indicating that the signal peptide is encoded by residues 386-436 (17 codons) and the mature peptide is encoded by residues 437-1066 (210 codons).[2] This is yet further confirmed by the sequence numbering associated with the polypeptide sequences provided in SEQ ID NOs: 5 and 6, in which the numbering begins at "-17" rather than "1," to indicated that the 17 amino acid signal peptide is not present in the mature protein. Although SEQ ID NO: 6 discloses a 227 amino acid

[1] The Office Action notes that Applicant's prior response asserted that no new matter had been added. Office Action at p.3. Applicants' statement regarding new matter was, and remains, true.
[2] These "feature keys" are provided for and defined at WIPO Standard ST.25, Table 5, as provided at M.P.E.P. § 2422.

polypeptide sequence, it is numbered from "-17" to "210" in recognition that only the positive numbered residues (1-210) are present in the mature protein. In light of this (redundant) disclosure, one of skill in the art would immediately recognize that residues 1 – 210 of SEQ ID NO: 6 was the mature form of FDF03-S1, as claimed in original Claim 2.

Accordingly, Applicants respectfully request withdrawal of the new matter rejection.

II. Rejection under 35 U.S.C. §101

All pending claims were rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. Specifically, it is alleged that the claims do not sufficiently distinguish over antigen-antibody complexes as they exist naturally, such as autoantibodies against FDF03-S1.[3] Independent Claims 7 and 32 are amended herein to indicate that the antibody (or fragment thereof) is "purified." Support for this amendment is found, *e.g.*, at p.19, ll.11-17; p.20, ll.21-23 and p.23, ll.14-15.

This amendments to Claims 7 and 32 to clarify that they relate to complexes other than those occurring in nature finds additional support at original Claim 15, which is a method claim involving "contacting a sample" with an antibody specific for a polypeptide derived from a polypeptide of the invention (e.g. SEQ ID NO: 6) to form such a complex. It is implicit in the active step of "contacting" that the components must be separate (*i.e.* not together in a natural setting) prior to said contacting. Original Claim 15 also requires that said contacting must involve a "sample," and one of skill in the art would understand that such a sample must be separate from an organism. As stated at page 5 of the specification, "sample" refers to, for example, "tissue or fluid **isolated from** an individual or from an *in vitro* cell culture constituents [sic], as well as samples obtained from laboratory procedures" (bolding added). It is apparent that Claim 15, involving a "sample" and a "contacting" step (reflecting the hand of man), does not encompass antigen-antibody complexes as they might exist in nature.

III. Rejection under 35 U.S.C. §102(a)

All pending claims were rejected under 35 U.S.C. §102(a) as allegedly being anticipated by **Adema *et al.* (WO 98/24906)**, as evidenced by Bost *et al.* (1988) *Immunol. Invest.* 17:577 and Bendayan (1995) *J. Histochem. Cytochem.* 43:881.

[3] No evidence or argument is provided to support the existence of any such autoantibodies, nor antibody-antigen complexes.

Applicants have previously pointed out that Adema *et al.* does not disclose the polypeptide of the present claims (*i.e.* SEQ ID NO: 6, or residues 1-210 of SEQ ID NO: 6), and thus cannot anticipate the claims.

In response, the current Office Action discusses the "high degree of sequence homology between the prior art polypeptide of FDF03 of SEQ ID NO: 2 [of Adema *et al.*] and instant FDF03-S1 consisting of SEQ ID NO: 6" (Office Action at p.6), and refers to a sequence alignment indicating 19 mismatches and 15 conservative changes.[4] The Office Action then discusses the possibility that the antibodies of Adema *et al.* would cross-react with the instant FDF03-S1 of SEQ ID NO: 6.

Neither of these observations, even if accepted as true, has any bearing on Applicants' argument that Adema *et al.* does not anticipate the claims. All pending claims require the presence of a polypeptide consisting of SEQ ID NO: 6 or residues 1-210 of SEQ ID NO: 6. Adema *et al.* does not disclose either polypeptide, and thus cannot anticipate any claim.

IV. Rejections under 35 U.S.C. §102(e) and §103(a)

Claims 7 and 32 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by **Escobedo *et al.*** (U.S. Pat. App. Pub. No. 2002/0076761), and all pending claims were rejected under §103(a) as allegedly being obvious over Escobedo *et al.* in view of **Harlow *et al.*** (Antibodies: A Laboratory Manual, 1988, pages 139-147 and 626-630) and **Campbell** (Monoclonal Antibody Technology, 1985, Elsevier Science Publishers, Chapter 1, pages 1-32). In the interest of efficiency, Applicants will argue against both of these rejections together since the argument is based solely on the inadequacy of Escobedo *et al.* as a reference.

Currently pending independent Claims 7 and 32 recite complexes comprising polypeptides "*consisting of* the amino acid sequence of SEQ ID NO: 6" and "*consisting of* the amino acid sequence of residues 1 – 210 of SEQ ID NO: 6", respectively. Although Escobedo *et al.* discloses at SEQ ID NO: 21 a 291 amino acid polypeptide that *includes* the sequence of SEQ ID NO: 6, and therefore residues 1 – 210 of SEQ ID NO: 6, it does not disclose a polypeptide *consisting of* either of these sequences. As pointed out in Applicants' previous response, neither Harlow *et al.* nor Campbell supply the polypeptides of the claims either.

Because both the §102(e) and §103(a) rejections are critically dependent on the allegation that Escobedo *et al.* discloses the polypeptides of the claims, and it does not,

[4] The discussion of a "high degree of homology" is an admission that the sequence of Adema *et al.* is not identical to the claimed polypeptide sequences, as is also readily apparent from the sequence alignment attached to the Office Action.

Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §102(e) and §103(a).

CONCLUSION

Applicants' current response is believed to be a complete reply to all the outstanding issues of the latest Office Action. Further, the present response is a *bona fide* effort to place the application in condition for allowance or in better form for appeal. Accordingly, Applicants respectfully request reconsideration and passage of the amended claims to allowance at the earliest possible convenience.

Applicants hereby authorize the Office to charge any fees that may be due, and to credit any refunds, to Deposit Account No. 04-1239.

If the Examiner believes that a telephonic conference would aid the prosecution of this case in any way, please call the undersigned.

Respectfully submitted,

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